

**CLAIMS**

5 What is claimed is

1. A method for evaluating the dynamic biological state of a patient, said method, which involves measuring several elements or substances present in blood and interpreting results of performed measures, comprising the following steps:

(1°) providing the blood previously taken from a patient;

(2°) determining in vitro, from said blood, hematic substances as metabolic and/or tissular parameters:

- number of red blood cells (GR),

- number of leukocytes (GB),

- hemoglobin (HG),

- number of neutrophils,

- number of eosinophils,

- number of lymphocytes,

- number of monocytes,

- number of platelets,

- lactate dehydrogenase (LDH),

- creatine phosphokinase (CPK),

- thyroid-stimulating hormone (TSH),

- alkaline phosphatases,

- liver (H1 and H2), bone (O1) and/or intestine (I1, I2 and I3) isoenzymes,

- osteocalcin,

- potassium and calcium, and

optionally, at least one of the following substances:

- carcinoembryonic antigen (CEA),

- one or several CA15-3, CA125 and CA19-9 markers,

- acid phosphatases, in particular prostatic acid phosphatase (PAP),

- prostate specific antigen (PSA),

- hourly sedimentation rate (ESR<sub>1</sub>),

- bihourly sedimentation rate (ESR<sub>2</sub>),

- thyroid hormones, in particular triiodothyronine (FT3) and thyroxine (FT4),

-  $\gamma$ -glutamyl transpeptidases,

- transaminases,

- chlorides and sodium, and

- adrenocorticotrophic hormone (ACTH);

(3°) measuring, from step (2°), at least one index selected from the group consisting of following indexes J1-J157:

- J1 the so-called genital ratio index, which is the ratio red blood cells/leukocytes,
- 5 J2 the so-called genital-thyroid ratio index, which is the ratio neutrophils/lymphocytes,
- J3 the so-called adaptation index, which is the ratio eosinophils/monocytes, J3 being such that  $J3 = \text{eosinophils/monocytes} = \text{ACTH/FSH}$ ,
- J4 the so-called thyroid index, which is the ratio LDH/CPK,
- 10 J5 the so-called estrogenic index, which is the ratio TSH/osteocalcin,
- J6 the so-called growth index, which is the ratio bone isoenzymes of the alkaline phosphatases/osteocalcin, (O1/osteocalcin),
- J7 the so-called turnover index, which is the product  $\text{TSH} \times \text{O1}$
- J8 the so-called fibrosis index, J8 being defined by the relation
- 15  $J8 = (\text{TSH})^2(\text{osteocalcin})^3/100$ ,
- J9 the so-called index of thyroid involvement, which is the ratio CA15-3/CEA,
- J10 the so-called index of follicular involvement, which is the ratio CA125/CEA,
- 20 J11 the so-called index of metabolic-hypothalamic involvement, which is the ratio CA19-9/CEA,
- J12 the so-called pancreatic index, which is the ratio PAP/PSA,
- J13 the so-called global TRH index of adaptation, which is the ratio CA19-9/TSH,
- 25 J14 the so-called index of leukocytes mobilization, J14 being defined by the relation  $J14 = (\text{platelets} \times \text{neutrophils} \times \text{HG})/(30 \times \text{leukocytes})$ ,
- J15 the so-called index of platelets mobilization, J15 being defined by the relation  $J15 = \text{platelets}/(60 \times \text{red blood cells})$ ,
- J16 the so-called index of thyroid reactivating activity, which is the ratio
- 30 monocytes/lymphocytes,
- J17 the so-called structure/function ratio index, J17 being defined by the relation  $J17 = (\text{neutrophils} + \text{basophils} + \text{monocytes})/(\text{eosinophils} \times \text{lymphocytes})$ ,
- J18 the so-called index of estrogenic fraction #1, which is the ratio
- 35 lymphocytes/osteocalcin,
- J19 the so-called index of estrogenic fraction #2, which is the ratio neutrophils/monocytes,
- J20 the so-called index of metabolic estrogenic fraction, which is the ratio LDH/osteocalcin,
- 40 J21 the so-called index of thyroid mobilization of bone metabolism, which is the ratio LDH/bone isoenzymes fraction of the alkaline phosphatases,

- J22 the so-called index of thyroid mobilization of bone endocrine metabolism, which is the ratio TSH/bone isoenzymes fraction of the alkaline phosphatases,
- 5 J23 the so-called index of relative osteomuscular metabolic activity, which is the ratio CPK/bone isoenzymes fraction of the alkaline phosphatases,
- J24 the so-called index of thyroid bone metabolic activity, which is the ratio CPK/osteocalcin,
- J25 the so-called catabolism/anabolism ratio index, J25 being the ratio J2/J1,
- J26 the so-called index of circulating cortisol, J26 being the ratio J25/J3,
- 10 J27 the so-called androgenic index, J27 being the ratio J1/J3,
- J28 the so-called adrenal cortex index, J28 being the ratio J26/J27,
- J29 the so-called index of adrenal cortex permissiveness, J29 being the ratio J1/J27,
- J30 the so-called index of aromatization of estrogens, J30 being the ratio J29/J1,
- 15 J31 the so-called level of catabolism, J31 being the ratio J4/J28,
- J32 the so-called level of anabolism, J32 being the ratio J31/J25,
- J33 the so-called level of metabolic activity efficiency, J33 being defined by the relation  $J33 = (J32 + J31) \times 100 / 2.25$ ,
- 20 J34 the so-called index of bone remodeling, which is the product TSH x J6,
- J35 the so-called index of nuclear membrane activity, J35 being the ratio J5/J6,
- J36 the so-called adjusted growth index, J36 being the ratio J6/J7,
- J37 the so-called anti-growth index, J37 being the ratio  $1/J36$ ,
- 25 J38 the so-called somatostatin index, J38 being the ratio J37/J26,
- J39 the so-called prolactin index, J39 being defined by the relation  $J39 = (J38/J6) \times \text{TSH}$ ,
- J40 the so-called level of membrane expansion, J40 being the product J31 x J36,
- 30 J41 the so-called level of structural expansion, J41 being the product J32 x J35,
- J42 the so-called apoptosis index, J42 being the ratio J41/J40,
- J43 the so-called adjusted apoptosis index, J43 being the ratio J42/J35,
- J44 the so-called level of membrane fracture, J44 being defined by the relation  $J44 = J33 / (\text{TSH} \times J7)$ ,
- 35 J45 the so-called necrosis index, J45 being the ratio J44/J42,
- J46 the so-called level of activity of total androgens, J46 being the product J5 x J1
- J47 the so-called rate of adrenal cortex androgens, J47 being defined by the relation  $J47 = J46 / (1 + J27)$ ,
- 40 J48 the so-called rate of genital androgens, J48 being defined by the relation  $J48 = (J46 - J47)$ ,
- J49 the so-called progesterone index, J49 being defined by the relation

- J49 =  $J5/(J48 \times J3)$ ,
- J50 the so-called level of activity of genital estrogens, J50 being defined by the relation  $J50 = J5/(1 + J30)$ ,
- J51 the so-called rate of aromatized estrogens, J51 being defined by the relation  $J51 = J5 - J50$ ,
- JJ53 the so-called folliculin index, J53 being defined by the relation  $J53 = 20 \times (J5/J49)$ ,
- J54 the so-called insulin index, J54 being defined by the relation  $J54 = (100 \times J25)/(J7 \times TSH)$ ,
- J55 the so-called demyelination index, J55 being defined by the relation  $J55 = J54/(J36 \times J6)$ ,
- J56 the so-called index of DNA fracture, J56 being defined by the relation  $J56 = (100 \times J5 \times J6 \times J41)/(J7 \times J35 \times J42 \times J45)$ ,
- J57 the so-called index of nucleocytoplasmic pathogenicity, J57 being defined by the relation  $J57 = (1.7 \times J56)/J44$ ,
- J58 the so-called index of cellular fracture, J58 being defined by the relation  $J58 = 2.5 \times J44 \times J56/J45$ ,
- J59 the so-called index of carcinogenesis, J59 is the ratio  $J57/J42$ ,
- J60 the so-called index of comparative carcinogenesis, J60 being defined by the relation  $J60 = (10 \times J58)/J43$ ,
- J61 the so-called index of active cellular permeability, J61 being defined by the relation  $J61 = J6 \times J34/J54$ ,
- J62 the so-called index of adjusted active cellular permeability, J62 being defined by the relation  $J62 = (J61 \times J29)/J26$ ,
- J63 the so-called index of passive cellular permeability, J63 being defined by the relation  $J63 = J45 \times J35 \times J68 \times 10$  (wherein J68 is defined as indicated below),
- J64 the so-called index of active intracellular osmolar gradient, J64 being defined by the relation  $J64 = 100 \times J54 \times J40 \times J35/J3$ ,
- J65 the so-called index of adjusted active intracellular osmolar gradient, J65 being defined by the relation  $J65 = (J64 \times J29)/J26$ ,
- J66 the so-called index of passive intracellular osmolar gradient, J66 being defined by the relation  $J66 = (10 \times J43 \times J53)/(J45 \times J8)$ ,
- J67 the so-called oxidation-reduction index, J67 being defined by the relation  $J67 = (100 \times J45 \times J40 \times J41 \times J54)/(J71 \times J8 \times J38)$ , (wherein J71 is defined as indicated below),
- J68 the so-called index of corticoadrenal adaptation/permissiveness, J68 being defined by the relation  $J68 = J26 - J29 - J28$ ,
- J69 the so-called adaptogenic index which is the ratio  $K/Ca$ ,
- J70 the so-called  $\beta$ MSH/ $\alpha$ MSH index, (differential melanocyte-stimulating hormones), J70 being the ratio  $J4/J69$ ,

- J71 the so-called apoptosis bis index, J71 being defined by the relation  
 $J71 = J35/(J36 \times J25)$ ,
- J72 the so-called amylosis index, J72 being defined by the relation  
 $J72 = (J38 \times J53 \times J55 \times TSH)/(J4 \times J5 \times J54)$ ,
- 5 J73 the so-called index of amylosis risk, J73 being the ratio  $J8/J67$ ,
- J74 the so-called index of insulin resistance, J74 being the ratio  $J38/J54$ ,
- J75 the so-called upstream index #1, J75 being the ratio  $J4/J9$ ,
- J76 the so-called upstream index #2, J76 being the ratio  $J4/J10$ ,
- J77 the so-called upstream index #3, J77 being the ratio  $J4/J11$ ,
- 10 J78 the so-called global upstream index #1, J78 being the ratio  $J75/J76$ ,
- J79 the so-called global upstream index #2, J79 being the ratio  $J75/J77$ ,
- J80 the so-called global upstream index #3, J80 being the ratio  $J76/J77$ ,
- J81 the so-called index of thyroid output #1, J81 being the ratio  $J4/TSH$ ,
- J82 the so-called index of free radicals, J82 being the ratio  $J67/J54$ ,
- 15 J83 the so-called adjusted index of free radicals, J83 being defined by the  
relation  $J83 = (J67 + J64)/(J54 + J74)$ ,
- J84 the so-called comparative index of free radicals, J84 being defined by the  
relation  $J84 = (J67 + (100 \times J40))/(J54 + J74)$ ,
- J85 the so-called index of free radical nocivity, J85 being defined by the  
20 relation  $J85 = ((J82 + J83 + J84) \times J56)/(3 \times J71)$ ,
- J86 the so-called adjusted apoptosis index (B), J86 being the ratio  $J71/J35$ ,
- J87 the so-called index of active histamine, J87 being defined by the relation  
 $J87 = (\text{eosinophils} \times \text{platelets} \times J3)/J52$ ,
- J88 the so-called index of potential histamine, J88 being defined by the  
25 relation  $J88 = (J87 \times J63)/(\text{potassium} \times J70)$
- J89 the so-called TRH index, which is the ratio  $TSH/FT4$ ,
- J90 the so-called index of relative intrathyroid TRH activity, which is the ratio  
 $FT3/FT4$ ,
- J91 the so-called index of carcinogenic expansion, J91 being the ratio  $J60/J59$ ,
- 30 J92 the so-called index of cancer potential, J92 being the product  
 $J91 \times J54 \times J85$ ,
- J93 the so-called adenosis index, J93 being the ratio  $J8/J91$ ,
- J94 the so-called ischemia reperfusion index, J94 being defined by the relation  
 $J94 = 10 \times J34 \times J43/J33$ ,
- 35 J95 the so-called thrombogenic index, J95 being defined by the relation  
 $J95 = 10 \times J34 \times J42 \times J45/J33$ ,
- J96 the so-called thrombotic index, J96 being defined by the relation  
 $J96 = J95 \times J87 \times J1/10$ ,
- J97 the so-called adjusted genital ratio index, J97 being defined by the relation  
40  $J97 = (J14 \times \text{Red cells})/(\text{Leukocytes} \times J15) = J14 \times J1/J15$ ,
- J98 the so-called musculotropic index, J98 being defined by the relation  
 $J98 = J97 \times (\text{CPK}/O1)$ ,

- J99 the so-called adjusted estrogenic index, J99 being defined by the relation  $J99 = (J5 \times (\text{osteocalcin} + 1) / (\text{osteocalcin} + 1 - J98))$ ,
- J100 the so-called genital androgeny index, J100 being defined by the relation  $J100 = (J98/J81) \times J99 \times (J97)^2 / (J3 + J97)$ ,
- 5 J101 the so-called comparative genital androgeny index, J101 being defined by the relation  $J101 = (2 \times (\text{TSH})^2 \times \text{CPK}) / (J4 \times \text{osteocalcin} \times \text{O1})$ ,
- J102 the so-called “starter” index, J102 being the ratio  $J14/J15$ ,
- J103 the so-called adjusted index of thyroid reactivating activity, J103 being the product  $J16 \times J2$ ,
- 10 J104 the so-called pro-inflammatory index, J104 being the product  $J103 \times J69$ ,
- J105 the so-called index of inflammation, J105 being the product  $J104 \times J45$ ,
- J106 the so-called comparative index of inflammation, J106 being defined by the relation  $J106 = J105 / (((\text{ESR}_2/2) + \text{ESR}_1)/2) / \text{ESR}_1$ ,
- J107 the so-called interleukin 1 index, J107 being defined by the relation
- 15  $J107 = (J16 \times J38) / (J103 \times J37)$ ,
- J108 the so-called DHEA index, J108 being defined by the relation  $J108 = (J29 \times J30 \times J47 \times J51 \times J98 \times 1000) / (J49 \times J27 \times J100)$ ,
- J109 the so-called serotonin index, J109 being defined by the relation  $J109 = (10 \times J102) / (J54 \times J74)$ ,
- 20 J110 the so-called adjusted demyelination index, J110 being the product  $J55 \times J102$ ,
- J111 the so-called expansiveness index #1, J111 being the ratio  $J36/J35$ ,
- J112 the so-called expansiveness index #2, J112 being the ratio  $J40/J41$ ,
- J113 the so-called global expansiveness index, J113 being defined by the
- 25 relation  $J113 = (J111 \times J112) / J45$ ,
- J114 the so-called ACTH index, J114 being the ratio  $J108/J26$ ,
- J115 the so-called PTH index, J115 being defined by the relation  $J115 = (\text{calcium} \times \text{osteocalcin} \times \text{TSH}) / J4$ ,
- J116 the so-called index of gonadotropic output, J116 being defined by the
- 30 relation  $J116 = 1 / (J1 \times J53)$ ,
- J117 the so-called index of pelvic congestion, J117 being defined by the relation  $J117 = (J59/J60) \times (J94/J33)$ ,
- J118 the so-called index of splanchnic congestion, J118 being the ratio  $J117/J14$ ,
- 35 J119 the so-called growth score index, J119 being defined by the relation  $J119 = (J6 \times J37) / (J36 \times J38)$ ,
- J120 the so-called GH growth score index, J120 being defined by the relation  $J120 = (J6 \times J37) / J36$ ,
- J121 the so-called TRH/TSH ratio index, J121 being the ratio  $J72/J93$ ,
- 40 J122 the so-called index of thyroid efficiency, J122 being the ratio  $J4/J2$ ,
- J123 the so-called index of relative thyroid efficiency, J123 being the ratio  $J122/J81$ ,
- J124 the so-called index of oxidation, J124 being defined by the relation

- J124 =  $(100 \times J36 \times J54 \times J122)/(J74 \times J26)$ ,
- J125 the so-called index of reduction, J125 being the ratio  $J124/J67$ ,
- J126 the so-called pro-amyloid index, J126 being the product  $J125 \times J74$ ,
- J127 the so-called index of amyloid risk, J127 being the ratio  $J8/J124$ ,
- 5 J128 the so-called index of thyroid output #2, J128 being the product  $J2 \times J4$ ,
- J129 the so-called comparative index of thyroid output, J129 being the ratio  $J128/J81$ ,
- J130 the so-called index of estrogenic fraction #3, J130 being the ratio  $1/J1$ ,
- J131 the so-called index of estrogenic fraction #4, J131 being the product
- 10 J18 x J19,
- J132 the so-called index of estrogenic fraction #5, J132 being the product  $J19 \times J130$ ,
- J133 the so-called general index of estrogenic fraction, J133 being the product  $J18 \times J19 \times J130$ ,
- 15 J134 the so-called index of estrogenic fraction #6, J134 being defined by the relation  $J134 = 1/(\text{osteocalcin} \times J2)$ ,
- J135 the so-called index of estrogenic fraction #7, J135 being the product  $J18 \times J19 \times J134$ ,
- J136 the so-called index of estrogenic fraction #8, J136 being the ratio
- 20 J2/osteocalcin,
- J137 the so-called general quantitative estrogenic index, J137 being the product  $(J18 + J19) \times (\text{leukocytes}/100)$ ,
- J138 the so-called index of specific estrogenic fraction, J138 being the product  $J5 \times (J98 + 1)$ ,
- 25 J139 the so-called comparative estrogenic index #1, J139 being the ratio  $J133/(J5 \times 100)$ ,
- J140 the so-called comparative estrogenic index #2, J140 being the ratio  $J133/(J99 \times 100)$ ,
- J141 the so-called global comparative estrogenic index, J141 being the ratio
- 30  $J133/(J5 \times J99 \times 100)$ ,
- J142 the so-called index of somatotropic estrogenic output, J142 being the ratio  $J133/J144$  (where J144 is defined as indicated below),
- J143 the so-called index of quantitative organotissular estrogenic output, J143 being the ratio  $J137/J144$  (where J144 is defined below),
- 35 J144 the so-called FSH index #1, J144 being the ratio  $J114/J3$ ,
- J145 the so-called LH index #1, J145 being the product  $J114 \times J27$ ,
- J146 the so-called FSH index #2, J146 being the ratio  $J145/J1$ ,
- J147 the so-called LH index #2, J147 being the product  $J144 \times J1$ ,
- J148 the so-called index of progesterone output, J148 being the ratio  $J49/J138$ ,
- 40 J149 the so-called ketonic index, J149 being the ratio  $J102/J54$ ,
- J150 the so-called index of total subliminal TRH, J150 being the product  $\text{TSH} \times (\text{CA19-9}) \times J90$ ,
- J151 the so-called index of active carcinogenesis, J151 being the product

- J59 x J113,  
 J152 the so-called comparative index of active carcinogenesis, J152 being the product J60 x J113,  
 J153 the so-called gonadotrophic index, J153 being the ratio TSH/J2,  
 5 J154 the so-called index of global tissular estrogenic fraction, J154 being the ratio J140/J139,  
 J155 the so-called index of muscle destruction, J155 being the ratio J36/J101,  
 J156 the so-called amyloid score index, J156 being defined by the relation  

$$J156 = (J2 \times J53 \times J72 \times J94 \times J110 \times J126 \times J127) / (J4 \times J5 \times J67 \times J19 \times J20),$$
  
 10 J157 the so-called adjusted necrosis index, J157 being the product LDH x J45;  
 and,  
 (4°) comparing at least one of the J1-J157 indexes with the corresponding result obtained according to steps (2°) and (3°) with human beings already  
 15 recognized as being healthy, in order to appreciate dynamically the biological state of the patient to be tested.
2. A method according to claim 1, wherein at least one abnormality is looked for at the level of indexes J1 to J157 of the patient.
  3. A method according to claim 1, wherein (i) at least one index from J1 to J24 and (ii) at least one index from J1 to J24 and (iii) at least one index from J25 to J157 are looked for in step (3°).
  - 20 4. A method according to any one of claims 1-3, wherein in step (3°) at least 8, 10 or 15 indexes J are measured.
  5. A method according to claim 1, wherein in step (3°) at least a portion of indexes J1-J157, which constitute the scores of functions involved in the symptomatology and/or pathology of the patient to be tested, is measured.
  - 25 6. A method according to claim 5, wherein said scores of functions involved in the symptomatology and/or pathology are selected from the group consisting of the scores of pregnancy, menstruation, cardiovascularity, thrombosis, Alzheimer's disease, atherosclerosis, cancer and sudden death risk.
  - 30 7. A method according to claim 1, wherein in step (4°) the indexes obtained for a patient to be tested are compared with corresponding median values determined from healthy subjects.
  8. A software product loadable in particular in the internal memory of a computer, comprises portions of computer code to perform steps (3°) and (4°) of the method as claimed in claim 1.
  - 35 9. A software product according to claim 8, comprising
    - (F) a form field for entering (i) the patient's name or code, (ii) his age, and (iii) his sex, on the one hand, and any known treatment followed by said patient formerly or at the present time, on the other hand;
    - 40 (G) a form field for entering (iv) one or several hematic parameters measured *in vitro* from the blood of the patient and (v) the date of the measures;



(H) a field including all the indexes from J1 to J157, (vii) their calculation mode and (viii) their median values determined from human beings who are recognized as healthy subjects ;

5 (I) a command for (ix) the calculation of one index J, of several indexes J or the totality of indexes from the hematic parameters of said field (B) obtained from the blood of the patient to be tested, and (x) for the comparison of the obtained value for at least one of said indexes J with its median value of field (C); and,

10 (J) means for classifying, visualizing, editing and/or printing the obtained result by implementing command (D) starting from fields (A), (B), and (C).

10. A software product according to claim 9, wherein each median value of an index J in an interval of normal values previously determined from subjects recognized as being healthy.

15 11. A software product according to claim 9 or 10, which comprises an instruction for recognizing and flagging up any abnormality constituted by a value of an index J which stands away from its median value or interval thereof.

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